REMARKS

For convenience, in the present response, Applicants will refer the Examiner to disclosure in the specification by referencing the appropriate paragraph numbers of the Substitute Specification that was submitted on May 3, 2002.

Status of the claims

Upon entry of these remarks, claims 85-91, 118-124, 148-180, and 183-186 will be pending in this application. The word "therapeutically" has been deleted from claims 85, 118, 148, 158, 166, and 174. Claims 148 and 158 have been amended to recite "a cell culture containing B lymphocytes." New dependent claims 183-186 have been added. Support for the new and/or amended claims may be found in the specification as filed, for example at paragraphs [0049], [0050], [0429] and [0518]. No new matter has been added by way of amendment, and Applicants respectfully request entry of these amendments.

Objections to the specification

Applicants have amended paragraph [0060] to recite cDNA "clone HNEDU15" and to indicate that the nucleotide sequence obtained by sequencing the HNEDU15 clone is given in SEQ ID NO:1. Support for this amendment may be found in the specification as originally filed, for example in paragraphs [0023] and [0072] . The status of U.S. Application Serial Number 09/176,200 has been updated in paragraphs [0730] and [0731] to indicate its issuance as U.S. Patent No. 6,509,173. Applicants submit these amendments address the Examiner's objections to the specification set forth in paragraphs 1-3 of Paper No. 16. Applicants respectfully request these objections be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner has maintained the rejection of claims 85-91, 118-124 and 148-180 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. The Examiner's rejection can be distilled into three main points as follows:

> (A) "The specification and the references made of record do not teach that neutrokine-alpha increases/decreases the proliferation, differentiation, or survival of all lymphocyte

cells (e.g. T cells)....The skilled artisan must resort to trial and error experimentation to determine if neutrokine-alpha increases, decreases, or does not affect the proliferation, differentiation, and survival of T lymphocytes. Such trial and error experimentation is considered undue." (see, Paper No. 16, page 4, lines 17-20 and page 5, lines 3-6);

(B) "Undue experimentation would be required of the skilled artisan to determine the optimal, quantity, duration, and route of administration of the anti-neutrokine-alpha antibody." (see Paper No. 16, page 5, lines 9-11 and page 7 lines 1-3); and

(C) The specification does not enable one skilled in the art to treat "all possible autoimmune disorders...which have different pathophysiologies....[U]ndue experimentation would be required of the skilled artisan to treat all possible autoimmune diseases by administering an anti-neutrokine-alpha antibody." (see Paper No. 16, page 9, lines 3-8 and page 10, line 22 to page 11, line 1).

Applicants will address each aspect of the rejection in turn. Applicants note that these three aspects do not correspond one to one with sections (i), (ii), and (iii) as set forth in pages 3-11 of the Office Action mailed June 3, 2003. Below, Applicants indicate how each section of this response addresses the Examiner's points (i), (ii), and (iii).

A. The Examiner acknowledges that the specification and references made of record teach that Neutrokine-alpha induces B cell proliferation, differentiation and survival, but maintains that "[t]he specification and the references made of record do not teach that Neutrokine-alpha increases/decreases the proliferation, differentiation, or survival of all lymphocyte cells (e.g., T cells)." (see, Paper No. 16, page 4, lines 13-20). This argument corresponds to one of the main points in section (i) of the Office Action mailed June 3, 2003.

Applicants respectfully disagree. As detailed in the declaration under 37 C.F.R. § 1.132 by David Hilbert submitted herewith (hereinafter "the Hilbert Declaration"), Neutrokine-alpha has activity on lymphocytes, both B and T lymphocytes. Furthermore, this activity is taught in the specification (see, e.g., the specification in paragraphs [0040], [0051], [0077], [0153], [0156], [0620], [0622] and Examples 6 and 7) and corroborated by

the post-filing date literature such as the references cited in the Hilbert Declaration[1]. However, for the sake of facilitating prosecution, Applicants have amended claims 148 and 158 so as to replace the term "lymphocyte" with the term "B lymphocyte." Applicants state for the record, as noted in the Interview Summary dated April 14, 2003 in related US Application serial number 09/507,968, that this amendment is not a concession that Neutrokine-alpha does not have activity on T lymphocytes (see below). Moreover, Applicants maintain that it would not require undue experimentation to determine if antagonistic anti-Neutrokine-alpha antibodies inhibit Neutrokine-alpha-mediated activity on B cells and/or T cells.

Accordingly, Applicants respectfully request that this aspect of the rejection under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

B. The Examiner contends that, "undue experimentation is required to determine the optimal quantity, duration and route of administration of an antagonistic anti-Neutrokine-alpha antibody" (see Paper No. 16, page 5, lines 9-11 and page 7 lines 1-3). This argument corresponds to one of the two main points in each of sections (i), (ii) and (iii) of the Office Action mailed June 3, 2003. It is the Examiner's contention that undue experimentation is required (a) to determine the quantity, duration and route of administration and (b) to administer an antibody. Applicants will address points (a) and (b) in turn. Additionally, the Examiner maintains that the specification does not enable the skilled artisan to "determine the effect the antibody would have throughout the body." (see Paper No. 16, page 5, lines 15-16 and page 7, lines 3-4). Applicants will address this aspect of the rejection in section (c) below.

(a) Determination of optimal quantity, duration and route of administration

Applicants direct the Examiner's attention to section 2164 of the M.P.E.P., (8th edition, revision 1) which states that:

> If a statement of utility in the specification contains within it a connotation of how to use, and/or the art recognizes that standard modes of administration are known and contemplated, 35 U.S.C. 112 is satisfied. *In re Johnson*, 282 F.2d 370, 373, 127 USPQ 216, 219 (CCPA 1960); *In re Hitchings*, 342 F.2d 80, 87,

[1] A copy of each of the references cited in The Hilbert Declaration has been provided to the US Patent Office in conjunction with an Information Disclosure Statements submitted with the present Response or submitted previously.

> 144 USPQ 637, 643 (CCPA 1965). See also *In re Brana,* 51 F.2d 1560, 1566, 34 USPQ2d 1437, 1441 (Fed. Cir. 1993).
>
> For example, it is not necessary to specify the dosage or method of use if it is known to one skilled in the art that such information could be obtained without undue experimentation. If one skilled in the art, based on knowledge of compounds having similar physiological or biological activity, would be able to discern an appropriate dosage or method of use without undue experimentation, this would be sufficient to satisfy 35 U.S.C. 112, first paragraph. The applicant need not demonstrate that the invention is completely safe. See also M.P.E.P. § 2107.01 and § 2107.03.

Applicants submit that as of the earliest effective priority date of the present application there have been art recognized standards for determining the "optimal, quantity, duration, and route of administration" of an antibody. Illustrative of this point, Box 5 from Waldmann, TA, (2003) "Immunotherapy: Past, Present and Future" *Nature Medicine* 9:269-277, a copy of which is attached hereto as Exhibit 1, shows that several monoclonal antibodies were already approved by the United States Food and Drug Administration for administration to humans or in late stage human clinical trials at the time of the earliest effective priority date of the present application. This demonstrates that there were art recognized methods for determining the optimal, quantity, duration, and route of administration" of an antibody for administration to human (clinical trials) and animal subjects (pre-clinical experimentation). Therefore, Applicants submit the application meets the enablement standards under 35 U.S.C. § 112, first paragraph.

Applicants specifically address the Examiner's statement that "[a]lthough the claimed method utilizes routine techniques, the results of the method are unpredictable and complex when combined with the step of administering an-anti-neutrokine-alpha antibody." (see Paper No. 16, page 7, lines 15-17) with the following arguments. According to the Federal Circuit, "a considerable amount of experimentation is permissible, if it is merely routine" *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Jackson*, 217 USPQ 804 (Board of Patent Appeals and Interferences, 1982)). Additionally, Applicants remind the Examiner that while the predictability of the *art* can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the *result* of the experiment is not a consideration. Indeed, the Court of Custom and Patent Appeals has specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue in *In re Angstadt*, 190 USPQ 214 (C.C.P.A. 1976):

> [If to fulfill the requirements of 112, first paragraph, an applicant's] disclosure must provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction whether the claimed product will be obtained, . . . then all "experimentation" is "undue" since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act. .

Id. at 219 (emphasis in the original). As Judge Rich explained in *In re Vaeck*, 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991), the statutory enablement requirement is satisfied if the specification "adequately guides the worker to *determine*, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility" (emphasis provided). Because methods of determining the optimal quantity, duration and route of administration of an antibody were known in the art as earliest effective priority date of the present application, Applicants submit that one skilled in the relevant art could *determine*, without undue experimentation, the optimal quantity, duration and route of administration of an antagonistic anti-neutrokine-alpha antibody, the enablement requirement is fully satisfied. *In re Wands*, 858 F.2d at 738, 8 U.S.P.Q.2d at 1404; *Ex parte Mark*, 12 U.S.P.Q.2d 1904, 1906-1907 (B.P.A.I. 1989).

Thus, Applicants respectfully request that this aspect of the rejection under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn. Applicants address the enablement of administation of an antibody below.

(b) Administration of an antibody

The Examiner also indicates that neither the specification or any of the references teach administration of an *antibody*. The Examiner states that "undue experimentation would be required to deliver an anti-Neutrokine-alpha antibody to an individual" and "the state of the art at the time of the filing of the instant application was that problems were often encountered in the effort to use antibodies, particularly monoclonal antibodies, as clinical reagents." (see Paper No. 16, page 9, lines 17-19). The Examiner supports her statements with reference to articles by Ballow and Nelson[2] and Moore[3] which report that

[2] Ballow, M and Nelson, R, *JAMA* (1997) 278:2008-2017
[3] Moore, *Clin. Chem.* (1989) 35:1849-1853, reference U on PTO-892 sent with the Office Action mailed June 3, 2003.

administration of non-human antibodies to humans can induce immune responses against the administered foreign antibody, that antibodies may have either a low affinity or poor half-life, and that production of sufficient quantities of an antibody for therapeutic use was a challenge.

The "problems" encountered in the development of therapeutic antibodies relied on by the Examiner to support this rejection are related to either the safety or efficacy of the antibody or to the production of quantities sufficient for commercial scale manufacturing. In response, Applicants submit that such concerns are not appropriate considerations for patentability but rather are the concerns of the United States Food and Drug Administration and refer the Examiner to M.P.E.P. § 2107.03, subheading V entitled "Safety and Efficacy Considerations:"

> **V. SAFETY AND EFFICACY CONSIDERATIONS**
>
> The Office must confine its review of patent applications to the statutory requirements of the patent law. Other agencies of the government have been assigned the responsibility of ensuring conformance to standards established by statute for the advertisement, use, sale or distribution of drugs.

Moreover, recognition of the problem that the administration of non-human (foreign) antibodies to human subjects may induce an anti-foreign antibody immune response (which, in turn, may reduce the circulating half life of the foreign antibody) has not prevented the Food and Drug Administration, from approving (and continuing to approve) non-human or chimeric antibodies for use in human patients (see, Box 5 from Waldmann, TA, (2003) "Immunotherapy: Past, Present and Future" *Nature Medicine* 9:269-277, a copy of which is attached hereto as Exhibit 1. Thus, even if such concerns over the safety or efficacy of a therapeutic product were relevant to the patentability of the claimed methods, Applicants submit that the existence of such "problems" should not bar patentability.

Additionally, Applicants submit that the ability/inability to manufacture the antibodies used in the method of treatment in a large-scale setting suitable for commercial manufacture is immaterial to the patentability of the pending claims under 35 U.S.C. § 112, first paragraph. The enablement requirement of 35 U.S.C. § 112, first paragraph requires that the specification enable one skilled in the art to "make and use" the invention; it does not require that the specification enable the manufacture of enough product for a

commercially successful venture, or of enough product to treat a specified number of patients. This sentiment is echoed in the M.P.E.P. in § 2133.03(c). (in the context of the on sale bar of 35 U.S.C. § 102(b): "The invention need not be ready for satisfactory commercial marketing for sale to bar a patent. *Atlantic Thermoplastics Co. v. Faytex Corp.*, 970 F.2d 834, 836-37, 23 USPQ2d 1481, 1483 (Fed. Cir. 1992)"). Thus, Applicants submit that this basis of the rejection under 35 U.S.C. § 112, first paragraph should be reconsidered and withdrawn.

(c) Effects throughout the body

The Examiner indicates that the specification does not enable the skilled artisan to "determine the effect the antibody would have throughout the body." (see Paper No. 16, page 5, lines 15-16 and page 7, lines 3-4). In response, Applicants respectfully submit that a description of the effects an anti-Neutrokine-alpha antibody has throughout the body is unnecessary. Indeed, it is well established that an Applicant is not required to set forth the mechanisms through which the invention functions, nor is the Applicant required to even know how or why an invention works. See e.g., *Newman v. Quigg*, 11 U.S.P.Q.2d 1340, 1345 (Fed. Cir. 1989); *Diamond Rubber Co. v. Consolidated Rubber Tire Co.*, 220 U.S. 428, 435-36, 55 L. Ed. 527, 31 S. Ct. 444 (1911); *Fromson v. Advance Offset Plate Inc.*, 720 F.2d 1565, 1570, 219 U.S.P.Q. (BNA) 1137, 1140 (Fed.Cir. 1983). Moreover, the United States Court of Appeals for the Federal Circuit explicitly affirmed "[t]he PTO is not a guarantor of scientific theory and... it is not the province of the PTO to ascertain the scientific explanation." See, *In Re Newman*, 782 F.2d 971, 974 (1986).

Nonetheless, Applicants have provided ample information as to a mechanism by which an anti-Neutrokine-alpha antibody may work to treat autoimmune disease, i.e., through the inhibition of lymphocyte activity. As indicated in the Hilbert Declaration, one skilled in the art would appreciate the ability of an antagonistic anti-Neutrokine-alpha antibody to act as an immunosuppressant which can be used to alleviate the symptoms of autoimmune disease. Furthermore, paragraph 5 of the Hilbert Declaration indicates that other immunosuppressants used to treat autoimmune diseases act systemically and are not designed to target cells in particular locations of the body. Applicants submit that further information pertaining to the effects an anti-Neutrokine-alpha antibody has throughout the body or the location of B lymphocytes whose proliferation, differentiation or survival has been inhibited is not required for patentability under 35 U.S.C. § 112. Moreover, as

argued in Applicants response of May 3, 2002, medical doctors treating patients with autoimmune disease would be able to determine, without undue experimentation whether the symptoms of a given autoimmune disease have been alleviated, irrespective of information pertaining to the location in the body of lymphocytes whose activity has been inhibited by the administered antagonistic anti-Neutrokine-alpha antibody. Accordingly, Applicants respectfully request that this basis of the rejection under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

C. The Examiner contends that the specification does not enable one of skill in the art to treat "all possible autoimmune disorders...which have different pathophysiologies" (see Paper No. 16, page 9, lines 3-8). This argument corresponds to one of the two main points in each of sections (ii) and (iii) of the Office Action mailed June 3, 2003. Applicants will address this rejection as it applies to (a) claims 118-124, 165, and 173, 174-180 directed to methods of treating individual autoimmune diseases and (b) claims 85-91 and 166-172 directed to methods of treating the genus of autoimmune disease with antagonistic anti-Neutrokine-alpha antibodies, in turn.

(a) Enablement of claims 118-124, 165, and 173, 174-180 directed to methods of treating individual autoimmune diseases

First, Applicants point out to the Examiner claims 118-124, 165, and 173, 174-180 are directed to methods of treating individual autoimmune diseases, namely, rheumatoid arthritis, and systemic lupus erythematosus and submit that at the very least, these claims are fully enabled and that this aspect of the rejection as it relates to claims 118-124, 165, and 173, 174-180 should be withdrawn. The specification teaches that Neutrokine-alpha antagonists can be used to treat autoimmune diseases (see, for example, paragraphs [0050] and [0620] in the substitute specification submitted with Applicants' Response of May 3, 2003) thereby informing one of skill in the art that either excess Neutrokine-alpha protein levels and/or excessive Neutrokine-alpha activity would be present in autoimmune diseases. Rheumatoid arthritis and systemic lupus erythematosus are specifically listed as autoimmune diseases that could be treated with antagonists of the invention (see, for example, the specification as filed at paragraphs [0047], [0050] and [0620]). Post filing-date data corroborates the objective enablement of Applicants' disclosure by confirming

that increased levels of Neutrokine-alpha correlate with murine models of autoimmunity[4]. More particularly, increased levels of Neutrokine-alpha have been observed in Rheumatoid Arthritis[5] and Systemic Lupus Erythematosus[6] patients. Both rheumatoid arthritis and systemic lupus erythematosus are diseases characterized by the presence of autoantibodies in patient sera arising from the inappropriate proliferation, differentiation and/or survival of autoreactive B cells. It has also been shown that administration of a Neutrokine-alpha antagonist, i.e., soluble forms of Neutrokine-alpha receptors such as TACI-Fc or BAFF-Receptor 3, alleviates the symptoms of autoimmune disease in murine models of autoimmunity[7,8]. Moreover, David Hilbert states in his declaration (submitted herewith) that the above described data "were used to support Human Genome Sciences' (HGS) successful Investigational New Drug (IND) Application that enabled the company to begin human clinical trials for the use of an antagonistic anti-neutrokine-alpha antibody, known as Lymphostat B™ antibody, in the treatment of Systemic Lupus Erythematosus" and that these same data will be used to support a second IND Application for the use of Lymphostat B™ antibody in the treatment of rheumatoid arthritis" (see, paragraph 15 of the Hilbert Declaration).

Based on the foregoing arguments, Applicants reiterate their request that the rejection of claims 118-124, 165, and 173, 174-180 directed to methods of treating specific autoimmune diseases, namely rheumatoid arthritis and systemic lupus erythematosus, under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement be reconsidered and withdrawn.

(b) Enablement of Claims 85-91 and 166-172 directed to methods of treating the genus of autoimmune disease

Applicants have previously argued that the specification teaches that Neutrokine-alpha has a stimulatory effect on lymphocytes and that antagonistic anti-Neutrokine-alpha antibodies that inhibit the stimulatory effect that Neutrokine-alpha has on lymphocytes would be useful in the treatment of the genus of autoimmune diseases, which by definition are diseases that occur when autoreactive B and/or T lymphocytes are stimulated.

---

[4] Gross et al., *Nature* (2000) 404:995-999 cited as reference A51 submitted August 20, 2001.
[5] Cheema et al., *Arthritis Rheum.* (2001) 44:1313-1319 cited as reference B5 submitted May 3, 2002.
[6] Zhang et al., *Journal of Immunology* (2001) 166:6-10 cited as reference A69 submitted August 20, 2001.
[7] Gross et al., *Nature* (2000) 404:995-999 cited as reference A51 submitted August 20, 2001.

The Examiner did not find this argument persuasive because (1) autoimmune disorders disclosed in the specification have different pathophysiologies; (2) "[i]ncreased B cell activity is not the only characteristic of autoimmune diseases and neutrokine-alpha is not the only stimulant of B cells"; and (3) even though a claim may encompass inoperative embodiments, the Examiner asserts that there are a significant number of inoperative embodiments and that undue experimentation would be required to determine the operative embodiments.

Applicants respectfully disagree and direct the Examiner's attention to the Hilbert Declaration submitted herewith which affirms and extends Applicants' arguments to date. In the Declaration, Dr. Hilbert confirms that autoimmune diseases result from the activity of autoreactive B lymphocytes, and T lymphocytes and that the pathologies observed in autoimmune diseases result from damage inflicted by autoreactive cytotoxic T cells (T_{CTL}) and/or autoantibodies secreted by autoreactive B lymphocytes. Dr. Hilbert states, in paragraph 3 of the Declaration, that "Each autoimmune disease is defined by the specificity of the autoimmune reaction for a given tissue and the resulting pathology associated with destruction of that tissue"; and in paragraph 4, he continues "even though different autoimmune diseases may have different pathologies, every autoimmune disease involves a common mechanism, i.e., autoreactive B and/or T cell activity". Thus, while it is true that different autoimmune diseases such as rheumatoid arthritis or Grave's disease have different pathophysiologies, both diseases stem from the activity of autoimmune lymphocytes.

Dr. Hilbert also indicates that autoimmune diseases are (and were, as of the earliest priority date of the present application) treated with immunosuppressive therapies that inhibit activated lymphocytes, irrespective of their location in the body (see paragraph 5 of the Hilbert Declaration; also Table 24-1 of the 1997 article by Ballow and Nelson[9] which indicates that cytotoxic agents such as azathioprine, methotrexate and cyclophosphamide are used to treat autoimmune diseases).

Dr. Hilbert explains anti-Neutrokine-alpha therapy will act as a lymphocyte immunosuppressant by blocking Neutrokine-alpha's ability to act as a co-stimulatory signal necessary for lymphocyte activation thereby blocking downstream events such as

---

[8] Kayagaki et al., BAFF/BLyS receptor 3 binds the B cell survival factor BAFF ligand through a discrete surface loop and promotes processing of NF-kappaB2. *Immunity* (2002) 10:515-24.

autoantibody secretion and autoreactive T_{CTL} activity. Like other non-specific immunosuppressive therapies, anti-Neutrokine-alpha treatment would be expected to alleviate the symptoms of autoimmune diseases, regardless of the pathophysiology (by eliminating or reducing the common root cause of autoimmune diseases – effector lymphocyte activity.

Lastly, Dr. Hilbert also states that even if Neutrokine-alpha only directly affected B lymphocyte activity, it would, more likely than not, be useful in the treatment of autoimmune diseases because an antagonistic anti-Neutrokine-alpha antibody, in optimal, quantity, duration, and route of administration" of an antibody addition to directly inhibiting B cell activity, could indirectly inhibit T cell activity. Direct inhibition of B lymphocyte activity would alleviate the damage induced by autoantibodies. Additionally, direct inhibition of B lymphocyte activity could lead to indirect inhibition of T lymphocyte activity because B lymphocytes, by virtue of their ability to act as antigen presenting cells, can function to activate T_H cells which in turn can help activate T_{CTL} cells.

In short, the statements made by Dr. Hilbert in his declaration address each point of the Examiner's rejection. The Hilbert Declaration indicates that, like prior art immunosuppressive regimens, antagonistic anti-Neutrokine-alpha antibodies are expected to be useful in the treatment of autoimmune disorders even if they have different pathophysiologies. Dr. Hilbert's Declaration also indicates that Neutrokine-alpha's ability to function as a co-stimulatory molecule for B and T lymphocytes makes it a central player in the activation of lymphocytes and that the inhibition of Neutrokine-alpha's activity would therefore be useful in the treatment of autoimmune disorders. Lastly, in light of Dr. Hilbert's declaration, Applicants submit that the number of inoperative embodiments encompassed by the claims are not as extensive as the Examiner supposed and that it would only require routine testing by those of skill in the art to determine which embodiments are operative and which embodiments are inoperative. Accordingly, Applicants respectfully request that this aspect of the rejection under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

It is sincerely believed that all aspects of the Examiner's rejection under 35 U.S.C. § 112, first paragraph have been addressed and either obviated or overcome. Applicants

---

[9] Ballow, M and Nelson, R, *JAMA* (1997) 278:2008-2017, reference V on PTO-892 sent with the Office Action mailed June 3, 2003.

respectfully request that the entirety of the rejection under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 85-91, 118-124 and 148-180 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for using the word "therapeutically" to describe the effective amount that of the anti-Neutrokine-alpha antibody that must be administered. Applicants respectfully disagree, but in the interest of facilitating prosecution, Applicants have deleted the word "therapeutically" from claims 85, 118, 148, 158, 166, and 174. Accordingly, Applicants respectfully request that this rejection under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

CONCLUSION

Applicants respectfully request that the amendments and remarks of the present Amendment be entered and made of record in the present application.

In view of the foregoing remarks, Applicants believe that this application is now in condition for allowance. An early Notice of Allowance is earnestly solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution, the undersigned can be reached at the telephone number indicated below.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to Deposit Account No. 08-3425.

Respectfully submitted,

Date: December 2, 2003

Kenley K. Hoover (Reg. No. 40,302)
Attorney for Applicants

Human Genome Sciences, Inc.
9410 Key West Avenue
Rockville, MD 20850
Telephone: (301) 610-5771

KKH/MS/vsr